REMARKS

Status of the Claims

Claims 1-35 are pending. Claims 7-20, and 23-35 were withdrawn from further consideration as being drawn to non-elected subject matter as a result of a restriction requirement.

By entry of this amendment, claims 2-35 have been canceled without disclaimer or prejudice. Applicants reserve the right to pursue the subject matter encompassed in the canceled claims in subsequent continuation or divisional applications.

Claims 1 has been amended by this amendment. New claims 36-70 have been added. Thus, claims 1, and 36-70 are currently under examination.

No new matter has been added by this amendment.

Support for amended claims and the new claims can be found in the specification, Table 1, Table 2, Table 5, Table 6 and the Sequence Listing. Note that SEQ ID NO: 6756 is the genomic sequence where SEQ ID NO: 7368 (201 nucleotides) can be found.

This amendment adds, changes and/or deletes claims in the instant application. A detailed listing of all claims that are, or were, in the application, irrespective of whether the claims remain under examination in the application, are presented with an appropriate defined status identifiers. See 37 C.F.R. §1.121(c).

Rejections under 35 USC §102(e)

Claims 21 and 22 are rejected under 35 USC §102(e) for allegedly being anticipated by Wang (US 2003/0204075 A9).

By entry of this amendment, claims 21 and 22 have been cancelled, thus making this rejection moot. The Examiner is respectfully requested to withdraw this rejection.

Rejections under 35 USC §112, first paragraph, written description

The claims are rejected under 35 USC §112, first paragraph, for allegedly being not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors, at the time the application was filed, had possession of the claimed invention.

As amended, the claims now specify a single polymorphism SNP hCV 8227677, rs 498055, within SEQ ID NO: 7368, which is associated with altered risk of developing Alzheimer's disease (AD).

Therefore, the rejections under 35 USC §112, first paragraph, for allegedly lack of adequate written description have been overcome. The Examiner is respectfully requested to withdraw the rejections.

Rejections under 35 USC §112, first paragraph, enablement

The claims are rejected under 35 USC §112, first paragraph, for allegedly being not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The Examiner cited several references such as *Hirschorn et al.*, in support of the alleged unpredictability of the art. Another reference cited by the Examiner, *Bertram et al.*, stated that they were not able to find association of the SNP at issue with AD in their samples. As such, the Examiner alleged that the specification has not provided any guidance to enable one with ordinary skills in the art to practice the instantly claimed invention.

It is well known that the Examiner bears the initial burden to make a *prima facie* case that the claims are enabled in the specification. As stated above, the claims have been amended such that they recite one specific SNP that is to be detected in its association with AD. In that regard, Applicants have provided sufficient data analysis in the examples that the SNP at issue has been associated with AD, as shown in the Examples section, and in the tables of the instant application.

With respect to the references cited by the Examiner, contrary to the Examiner's characterization, they in fact support and bolster the results taught in the instant invention. As stated in *Hirschorn*, "associations can be real but nonetheless not reproducible if the underlying genetic is weak. If the subsequent studies are small in size, they will be underpowered to reliably detect weak effects and, therefore, fail to achieve significance." *Hirschorn*, Genetics in Medicine 2002, 4:45-61, at page 55. Further, *Hirschorn* teaches that "failure to observe the magnitude of effects seen in the first study should not be taken as a repudiation of the association." *Ibid.*

As an example, the *Bertram* study cannot be viewed as a "repudiation" of the disease association results taught in the instant invention, for the following reasons: First, *Bertram* uses family based samples, which are known to have increased risk allele frequency in unaffected family

members relative to the allele frequency in the general population. In contrast, the sample sets in the instant invention came from the general population. Second, the characterization of the unaffected control samples in *Bertram* was based on self assessment or a telephone interview, thereby increasing the chance of misclassification. It is important to note that misclassification in this group has a stronger impact than in the general population because family members of the Alzheimer's disease patients are at higher risk for the disease. Third, the family based sample sets included subjects with both early- and late-onset Alzheimer's disease, resulting in a further reduction of power. Thus, these factors may lead to the difference that the meta-analysis of the case-control sample sets in the instant invention confirms the significant association of the SNP (rs498055) with AD, while the family based study in Bertram may not have sufficient power to assess the association of the SNP with AD.

Therefore, the rejections under 35 USC §112, first paragraph, for allegedly lack of enablement have been overcome with the claims amendment and in light of the remarks above. The Examiner is respectfully requested to withdraw the rejections.

In conclusion, in light of the amendments and remarks above, Applicants submit that the present application is fully in condition for allowance. Early notice to that effect is earnestly requested.

The Examiner is invited to contact the undersigned via telephone if a phone interview would expedite the prosecution of the instant patent application.

Respectfully submitted,

By: 

Ben Wang, Reg. No.: 41,420

Date: April 6, 2007

Celera
1401 Harbor Bay Parkway
Alameda, CA 94502
Tel: 510-749-4378
Fax: 510-749-1895